REMARKS

Rejection of Claims and Traversal Thereof

In the December 7, 2009 Office Action:

Claims 1, 3, 5-7 and 10 were rejected under 35 U.S.C. §103(a) as being unpatentable over Hancock (US Pub. No. 2002/0018776) in view of Baba, et al (Proc. Natl. Acad. Sci. USA, May 1999, vol. 96 pp. 5698-5703, hereinafter Baba; and

Claims 1, 3, 5-7 and 10 were rejected under 35 U.S.C. §103(a) as being unpatentable over Vezina (WO94/05300) in view of Baba.

These rejections are hereby traversed and reconsideration of the patentability of the pending claims is therefore requested in light of the following remarks.

Rejection under 35 U.S.C. §103(a)

1. Claims 1, 3, 5-7 and 10 were rejected under 35 U.S.C. §103(a) as being unpatentable over Hancock in view of Baba and according to the Office, the combination of Hancock and Baba defeats the patentability of the presently claimed invention. Applicants insist that such a combination does not establish a *prima facie* case of obviousness.

Hancock describes a composition that includes an antagonist of CXCR3 and an immune suppressant, wherein the composition **is used to reduce graft rejections**. It is important to recognize that Hancock only relates to the CXC3 receptor and provides a broad and extensive list of possible antagonist that would be effective to react at the CXCR3 receptor and used to reduce graft rejection, including small organic molecule, natural product, protein, peptide or peptidomimetic. The Office mistakenly believes that this Hancock reference discloses using an antagonist of the CCR5 receptor but it does not. It only describes an antagonist for the CXCR3 receptor. Clearly there is a very important difference between the CXCR3 receptor and CCR5 receptor and no scientist that has any knowledge of receptors would read the Hancock reference and determine that the activity at the CXCR3, to reduce graft rejection, could be replaced with the use of an antagonist at the CCR5 receptor. There is nothing in the Hancock reference that would even suggest that the CCR5 receptor is related to the reduction of graft rejection.

The CCR5 receptor binds to MIP-1α, RANTES and MIP-1ß. Notably the CXCR3 receptor binds to IFN-γ and I-TAC. This Hancock reference provides lists of each of the general grouping of the required CXCR3 antagonists, such as:

[0024] Preferably, the antagonist of CXCR3 function is a compound which is, for example, a small organic molecule, natural product, protein (e.g., antibody, chemokine, cytokine), peptide or peptidomimetic. Several molecules that can antagonize one or more functions of chemokine receptors (e.g., CXCR3) are known in the art, including the small organic molecules disclosed in, for example, international patent application WO 97/24325 by Takeda Chemical Industries, Ltd.; WO 98/38167 by Pfizer, Inc.; WO 97/44329 by Taijin Limited; WO 98/04554 by Banyu Pharmaceutical Co., Ltd.; WO 98/27815, WO 98/25604, WO 98/25605, WO 98/25617 and WO 98/31364 by Merck & Co., Inc.; Hesselgesser et al., *J. Biol. Chem.* 273(25):15687-15692 (1998); and Howard et al., *J. Medicinal Chem.* 41(13):2184-2193 (1998); proteins, such as antibodies (e.g., polyclonal sera, monoclonal, chimeric, humanized, human) and antigen-binding fragments thereof (e.g., Fab, Fab', $F(ab')_2$, Fv), for example, those disclosed in WO 98/11218 by Theodor-Kocher Institute and LeukoSite, Inc.; chemokine mutants and analogues, for example, those disclosed in U.S. Pat. No. 5,739,103 issued to Rollins et al., WO 96/38559 by Dana Farber Cancer Institute and WO 98/06751 by Research Corporation Technologies, Inc.; peptides, for example, those disclosed in WO 98/09642 by The United States of America. The entire teachings of each of the above cited patents, patent applications and references are incorporated herein by reference.

[0027] The term "natural product", as used herein, refers to a compound which can be found in nature, for example, naturally occurring metabolites of marine organisms (e.g., tunicates, algae), plants or other organisms, and which possesses biological activity, e.g., can antagonize CXCR3 function. For example, lactacystin, paclitaxel and cyclosporin A are natural products which can be used as anti-proliferative or immunosuppressive agents.

[0028] Natural products can be isolated and identified by suitable means. For example, a suitable biological source (e.g., vegetation) can be homogenized (e.g., by grinding) in a suitable buffer and clarified by centrifugation, thereby producing an extract. The resulting extract can be assayed for the capacity to antagonize CXCR3 function, for example, by the assays described herein. Extracts which contain an activity that antagonizes CXCR3 function can be further processed to isolate the CXCR3 antagonist by suitable methods, such as, fractionation (e.g., column chromatography (e.g., ion exchange, reverse phase, affinity), phase partitioning, fractional crystallization) and assaying for biological activity (e.g., antagonism of CXCR3 activity). Once isolated the structure of a natural product can be determined (e.g., by nuclear magnetic resonance (NMR)) and those of skill in the art can devise a synthetic scheme for synthesizing the natural product. Thus, a natural product can be isolated (e.g., substantially purified) from nature or can be fully or partially synthetic. A natural product can be modified (e.g., derivatized) to optimize its therapeutic potential. Thus, the term "natural product", as used herein, includes those compounds which are produced using standard medicinal chemistry techniques to optimize the therapeutic potential of a compound which can be isolated from nature

[0029] The term "peptide", as used herein, refers to a compound consisting of from about two to about ninety amino acid residues wherein the amino group of one amino acid is linked to the carboxyl group of another amino acid by a peptide bond. A peptide can be, for example, derived or removed from a native protein by enzymatic or chemical cleavage, or can be prepared using conventional peptide synthesis techniques (e.g., solid phase synthesis) or molecular biology techniques (see Sambrook, J. et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring Harbor, N.Y. (1989)). A "peptide" can comprise any suitable L- and/or D-amino acid, for example, common α-amino acids (e.g., alanine, glycine, valine), non-α-amino acids (e.g., β-alanine, 4-aminobutyric acid, 6-aminocaproic acid, sarcosine, statine), and unusual amino acids (e.g., citrulline, homocitrulline, homoserine, ornithine). The amino, carboxyl and/or other functional groups on a peptide can be free (e.g., unmodified) or protected with a suitable protecting group. Suitable protecting groups for amino and carboxyl groups, and means for adding or removing protecting groups are known in the art and are disclosed in, for example, Green and Wuts, "*Protecting Groups in Organic Synthesis*", John Wiley and Sons, 1991. The functional groups of a peptide can also be derivatized (e.g., alkylated) using art-known methods.

[0030] Peptides can be synthesized and assembled into libraries comprising a few to many discrete molecular species. Such libraries can be prepared using well-known methods of combinatorial chemistry, and can be screened as described herein or using other suitable methods to determine if the library comprises peptides which can antagonize CXCR3 function. Such peptide antagonists can then be isolated by suitable methods.

[0031] The term "peptidomimetic", as used herein, refers to molecules which are not polypeptides, but which mimic aspects of their structures. For example, polysaccharides can be prepared that have the same functional groups as peptides which can antagonize CXCR3. Peptidomimetics can be designed, for example, by establishing the three dimensional structure of a peptide agent in the environment in which it is bound or will bind to CXCR3. The peptidomimetic comprises at least two components, the binding moiety or moieties and the backbone or supporting structure.

Thus, it is evident that Hancock provides hundreds of different choices for the CXCR3 antagonist but there is no indication that a CCR5 receptor antagonist could be effective as reducing graft rejection. The few examples in Hancock are limited to mice that do not express the CXCR3 receptors or monoclonal antibodies that bind to the CXCR3 receptors.

Hancock is very concerned about an increase or continuous release of chemokines because they recruit more soldiers to the site of inflammation. To prevent this increase of chemokines the Hancock group included an immunosuppressant to reduce the immune response. The list of immunosuppressive agents is set forth in paragraph 64 and includes a multiplicity of different choices, as shown below:

> "The term "immunosuppressive agent", as used herein, refers to compounds which can inhibit an immune response. The immunosuppressive agent used in the invention can be a novel compound or can be selected from the compounds which are known in the art, for example,
>
> calcineurin inhibitors (e.g., cyclosporin A, FK-506),
>
> IL-2 signal transduction inhibitors (e.g., rapamycin),
>
> glucocorticoids (e.g., prednisone, dexamethasone, methylprednisolone, prednisolone),
>
> nucleic acid synthesis inhibitors (e.g., azathioprine, mercaptopurine, mycophenolic acid) and
> antibodies to lymphocytes or antigen-binding fragments thereof (e.g., OKT3, anti-IL2 receptor).
>
> Novel immunosuppressive agents can be identified by those of skill in the art using suitable methods, for example, screening compounds for the capacity to inhibit antigen-dependent T cell activation.
>
> [0065] The immunosuppressive agent used for co-therapy (e.g., co-administration with an antagonist of CXCR3 function) is preferably a calcineurin inhibitor. More preferably the immunosuppressive agent used for co-therapy is cyclosporin A."

Specifically, the Hancock group administers the immunosuppressive agent to lower the level of chemokines and prefers the use of cyclosporin A to induce this result. Clearly there is no guidance in the specification as to which immune suppressor is important among the laundry list of possible choices excepting the preferred Cyclosporin A.

According to the Office:

> Hancock teach a method for inhibiting the rejection of transplanted grafts comprising an effective amount of an antagonist of CCR5 and an effective amount of an immunosuppressive agent (see abstract and claims 1, 6 and 13). Immunosuppressive agents include rapamycin (see paragraph 60; addresses claims 1 and 3). AND
> Hancock does not teach TAK 779 (claims 1, 5 and 6)
>
> Baba et al teaches that TAK-779 is a small-molecule, nonpeptide that is a specific CCR5 antagonist (see title and abstract).
>
> To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the compositions of Hancock et al. and TAK 779 because TAK 779 is a small molecule that specifically antagonizes CCR5

Importantly, As stated above, the Office is wrong that the Hancock reference teaches the use of an antagonist of CCR5 **but instead states specifically that all antagonists are limited to the CXCR3 receptor. Applicants expect the Office to show where this reference discusses the CCR5 antagonist to reduce graft rejection.**

Just by reviewing Hancock, it is evident that the only time the CCR5 receptor was even discussed was in column 1, page 13, paragraph [0105] wherein it was found that the CCR5 receptor was found in 41% of the biopsies but that it was not associated with rejection. This was also true for the CCR3 receptor. Thus where is there any incentive to even consider a CCR5 antagonist.

Clearly, the Office is under the misconception that a skilled artisan would wish to change the CXCR3 antagonist with a CCR5 antagonist because there is no indication or suggestion in Hancock to work on an entirely different receptor. With the help of applicants' invention, the Office found the Baba reference which describes the use of TAK 779 as a CCR5 antagonist. Then, the Office proposes that the teachings of these two references render the presently claimed invention as obvious. Applicants vigorously disagree.

Under Graham, and as required by MPEP §§ 2111 and 2141.02, the Office must ascertain the differences between the claimed invention and the prior art, and must consider both the invention and **the prior art as a whole**. Thus, even in light of the *KSR* decision, **the Office must consider the inventions of any cited references in their respective entireties.** Certain individual features from the references may not be arbitrarily chosen (while equally arbitrarily discarding other disclosed features) to merely lump together disparate features of different references as a mosaic in an attempt to meet the features of the rejected claims. Thus, the Office is not allowed to pick and choose just certain parts of different references and combine them, **but instead, the references in their entirety must be considered.**

Further, applicants remind the Office that Section 2143.01 of the MPEP, as well as the ruling in *In re Ratti*, (270 F.2d 810 (CCPA 1959)) state that where a proposed modification or combination would change the **principle of operation of the prior art invention being modified**, then the teachings are not sufficient to establish a *prima facie* case of obviousness. Thus, a combination of references that fundamentally change the "basic principals" under which the prior art was designed to operate cannot support a finding of obviousness. According to the Board in *Ex Parte Vito Cellini*, (Appeal 2008-4104, BPAI 2008), "a change in the basic principles" refers to change that is fundamental in scope so as to **relates to scientific or technical principles of operation.**

Applicants insist that the suggested combination of Hancock and Baba will change the "basic scientific principles" of the Hancock reference. Clearly, the effect of antagonizing the CXCR5 receptor is very different from using a compound that antagonizes the CCR5 receptor. A skilled artisan looking for a way to reduce graft rejection would not look to a receptor used by HIV for entry into an activated T-cell.

Thus if the teachings of Babe is combined with Hancock, the **"basic scientific principles" of Hancock reference will be changed**. As such, the proposed combination does not establish a *prima facie* case of obviousness because the combination of references fundamentally change the "basic principals" under which the prior art was designed to operate. Thus, the suggested combination of references would require a substantial change in the elements of the prior art as well as a change in the basic scientific principals under which the prior art was designed to operate.

Further, the Hancock reference provides a laundry list of immunosuppressive agents but no guidance as to success of any of the compounds for the purpose of increasing beta-chemokines. The Office's contention that it would be obvious to make a composition comprising a G1 phase arresting agent and an antiviral agent that increases levels of beta-chemokines is similar to an "obvious to try" rejection. If this is the

situation, it is important for the Office to review the "*In re Kubin*" ruling decided on April 3, 2009 because it provides guidance showing that the presently claimed invention is not obvious. (See I*n re Kubin*,90 USPQ2d 1417 (Fed. Cir. 2009))

Specifically, the *Kubin* Court revisited the *In re O'Farrell* decision (*In re O'Farrell*, 853 F.2d 894(Fed Cir. 1988)) and discussed that to differentiate between proper and improper applications of "obvious to try," the O'*Farrell* Court outlined two classes of situations where "obvious to try" is erroneously equated with obviousness under §103. In the first class of cases:

> what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.

In such circumstances, wherein metaphorical darts at a board filled with combinatorial prior art possibilities, courts should not succumb to hindsight claims of obviousness.

The second class of *O'Farrell's* impermissible "obvious to try" situations occurs where

> what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.

Clearly the first class applies to the present invention. The cited prior art provides a laundry list of immunosuppressive agents but there is no guidance to go in the direction of applicants' claimed invention. Surely Hancock would never consider a treatment that increased the level of chemokines in combination with the described antagonists.

Importantly applicants have provided proof of the effectiveness of the presently claimed combination that not only shows increased levels of chemokines but reduced levels of HIV virus. The proposed combination does not teach or suggest these benefits.

Initially it should be noted that the present invention provides for combination of a CCR5 antagonist and the G1 phase arresting agent wherein the G1 phase arresting agent must in a sufficient amount to increase the level of chemokines and specifically the MIP-1α, MIP-1β and RANTES chemokines.

Applicants have surprisingly found that the addition of RAPA increases the level of chemokines as shown in Figure 3A, recreated below:

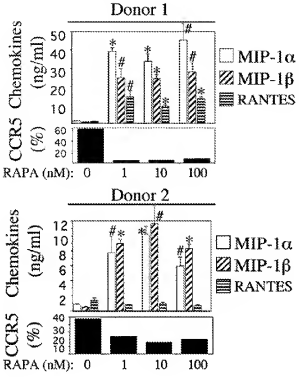


Figure 3A

As the Court stated in *Interconnect Planning Corp. v. Feil,* 227 USPQ 543 (Fed. Cir. 1985) "The invention must be viewed not with the blueprint drawn by the inventor, but **in the state of the art that existed at the time**," (emphasis added) The state of the art existing at the time of the invention was characterized by understanding that combining a CXCR3 antagonist and immunosuppressive agent caused a reduction of chemokines. Nothing in the combination hinted of an increase in chemokines. Moreover, there is no suggestion or teaching that this combination would effectively increase an immune response and reduce replication of HIV.

In light of the above discussion, applicants request reconsideration and the withdrawal of this rejection for obviousness

2. Claims 1, 3, 5-7 and 10 were rejected under 35 U.S.C. §103(a) as being unpatentable over Vezina in view of Baba. Applicants insist that such a combination does not establish a *prima facie* case of obviousness.

According to the Office, Vezina, et al (WO 94/05300) teaches the use of RAPA and an antiviral HIV agent that in combination with Baba defeats the patentability of the presently claimed invention.

According to the Office, Vezina, et al (WO 94/05300) teaches the use of RAPA and an antiviral HIV agent that defeats the patentability of the presently claimed invention. Applicants disagree because Vezina does not disclose teach or suggest the use of an antiviral agent **that inhibits entry of HIV into effected cells.** As previously stated, Vezina only teaches the use of **reverse transcriptase inhibitors or protease inhibitors** both of which are not effective until the enemy has passed over the moat, into the castle, through the door, and has taken over the castle or ready to take over every castle in the kingdom. (Attacking every T-cell in the system).

One of the major effects of the Vezina reference is the loss of CD4 cells because the cell replication is decreased. Vezina believes this loss of CD4 cells is acceptable, however, applicants know that the loss of CD4+ cells causes increased problems for subjects suffering with HIV because of the diminishment of immune response.

Reviewing the results of Example 2 of Vezina shows the emphasis on the inhibition of CD4 cells replications:

EXAMPLE 2.
In vitro incubation of rapamycin with $CD4^+$ human cells uninfected and infected with defective HIV-1.

TEST CELL CULTURES:

Different concentrations of rapamycin were tested on the following cell lines in culture:
-MT-4 ($CD4^+$ T lymphocytes);
-MT-2 (MT-4 cells infected with a defective HIV-1 HTLV III_B [Harada et al., Science 229: 563-566, 1985, enclosed herewith by reference];
-U937 (monocyte) (ATCC CRL-1593); and
-UHC8 (U937 infected with a defective HIV-1 HTLV III_B, R3 strain [Boulerice et al., J. Virol., 64, 1745-1755, 1990, enclosed herewith by reference].

It is evident from the results below that replication of infected cells CD4+ cells (MT-2 and UHC8) were inhibited, and thus, less T-cells are available to the immune system to combat the HIV virus. Clearly, this is a problem because of the diminishment of immune T cells that are required to overcome the negative effects of HIV.

Results are presented in Table 3 as percent of inhibition of cellular growth of infected and uninfected host cells:

Table 3

Rapamycin (ng/ml)	MT-4 (% inhibition)	MT-2 (% inhibition)	U-937 (% inhibition)	UHC8 (% inhibition)
0	0	0	0	0
0.01	39	49	24	48
0.1	78	85	76	83
1	87	--	--	87
10	81	85	78	91
100	82	86	82	62

The toxicity of the compound at 100 ng/ml through 0.1 ng/ml was greater than about 80% cellular inhibition both for uninfected and infected cells. Although, at 0.01 ng/ml, the infected cells seemed slightly more sensitive to rapamycin than the uninfected cells, it seems that the anti-HIV effect of rapamycin may be due primarily to its toxicity on the replication of the host cells (lymphocytes and monocytes).

Thus, the replication of T cells is decreased and the subject can be depleted of an important soldier of the immune system.

In sharp contrast, the present invention avoids the shortcomings of Vezina because the CD4 containing T-cells are not reduced but the cell viability is maintained with an increase of chemokines which provides for the maintenance of the cell viability but also a reduction of HIV replication as shown in Figure 5 A.

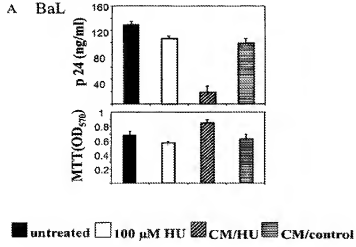


Figure 5

Figure 5 provides the results of using hydroxyurea as the G1 phase arresting agent. The antiviral activity of the supernatants collected from cultures of PBMCs that had been exposed to 100 μM HU for 7 days [supernatants referred to as conditioned medium (CM)] was evaluated in PBMCs infected with HIV-1 BaL and HIV-1 IIIb. Briefly, PHA-activated PBMCs were infected with each virus at 100 tissue culture 50% infective dose units ($TCID_{50}$)/10^6 PBMCs or 10 $TCID_{50}$/10^6 PBMCs for 2 h at 37°C. Infected cells were cultured in IL-2 medium alone, IL-2 medium with 100 μM HU, IL-2 medium containing 50% supernatant from HU-treated PBMCs (CM/HU), or IL-2 medium containing 50% supernatant from control-treated PBMCs (CM/control). On day 3 after infection, culture medium was replaced with fresh medium of the same kind as on day 1. Viral growth (measured by p24 levels in the supernatant) and cell viability (assayed by MTT) were determined on day 7 after infection.

It is evident that using the G1 phase arresting agent, hydroxyurea, maintained the cell viability including T cells and also reduced viral growth.

According to the Office, the Baba reference teaches the use of TAK 779 and proposes that it would be obvious to a skilled artisan to combine Vezina with Baba. Applicants insist that this general statement by the Office relating to HIV and pharmaceuticals is totally without merit. On logical grounds, given the possibility of adverse drug-drug interaction, the added constraint of dealing with different solubilities, bioavailability, biocompatibility, etc. and other practical difficulties of cocktail formulation, the *prima facie* obviousness of such approach is not at all evident as the "general proposition" put forward by the Office. Further, it is imperative that the Office recognizes that there are no working examples in Vezina that shows a combination of RAPA with an antiviral agent so the proposed combination of drugs has not been shown to be effective in the treatment of HIV.

Applicants reiterate that the *Kubin* decision is relevant for the proposed combination. As stated above, the second class of *O'Farrell's* impermissible "obvious to try" situations occurs where

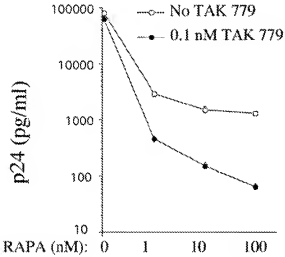
> what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.

Clearly this second class applies to the present invention. The cited prior art provides broad general statements but there is no guidance to go in the direction of applicants' claimed invention. Vezina has no working examples that include a combination of an anti viral agent in combination with RAPA, whether it

is AZT or TAK 779. Thus, there may be general guidance but no indication as to what direction would be effective.

Clearly, applicants have shown improvement far surpassing any results shown in Vezina or Baba. Applicants have provided proof of the effectiveness of the presently claimed combination that includes a G1 phase arresting agent in combination with an agent that stops the HIV virus before entry into the cell.

As shown in Figure 6 of the application, and recreated below for ease of discussion,



it is evident that there is impressive efficacy with the combination of RAPA and TAK 779. Clearly, 0.1 nM TAK-779 shows little antiviral activity and the results shown in Figure 4 (as set forth in the specification) indicate that administering RAPA alone reduces the level of P24 to nanograms/ml amounts. However, the combination of both agents reduces the levels of p24 to picograms/ml. Thus, the combination provides for a surprising reduction in replication of HIV-1.

Notably, by using the G1 phase arresting agent in combination with an antiviral that prevents the introduction of the virus into the cell, the addition of extra chemokines that block the landing sites maintains the availability of the t-cell and reduce infections.

This impressive efficacy is also shown in Figure 7 when hydroxyurea is combined with TAK 779 as shown below:

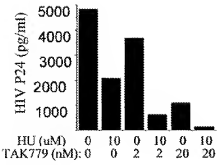


Figure 7

According to the Office, a skilled artisan would read the Baba reference and immediately disregard use of AZT of Vezina and instead use TAK 779 even if Vezina never shows the effectiveness of such combination. Applicants question where in either reference is there any suggestion that the proposed combination would be effective? There is none and the Office cannot speculation on such a combination, unless of course the Office is using applicants' specification as a blue print to go looking for ingredients. This type of hunting expedition would be using impermissible hindsight which is still considered unacceptable because the *KSR* Court expressly stated that a flexible TSM test remains the primary guarantor against **a non-statutory hindsight analysis such as the Office is using in the presently claimed invention.**

On July 21, 2008, the Federal Circuit expanded on post *KSR* establishment of a *prima facie* case of obviousness and stated in *Eisai Co. Ltd v Dr. Reddy Laboratories* 87 USPQ2d 1452 (Fed Cir 2008) that (1) *KSR* assumes a starting reference point, prior to the time of the invention, from which a skilled artisan might identify a problem and pursue potential solutions; (2) that the record up to the time of the invention would give some reason to make particular modifications; and (3) the record would provide some reason to narrow the prior art universe to a "finite number of identified and predictable solutions." Notably the *Eisai* Court further stated the "to the extent that an art is unpredictable, as in the chemical arts often are, *KSR's* focus on these 'identified, predictable solutions' may present a difficult hurdle because potential solutions are less likely to be genuinely predictable.

Applicants insist that after a review of the new guidelines for determination of obviousness and recent relevant case law, the Office cannot establish a *prima facie* case of obviousness and as such, applicants request that the rejection under 35 U.S.C. §103(a) be withdrawn.

Rejoinder of Method Claims

In accordance with Office guidelines recited in MPEP Section 821.04, when the elected product claims are found to recite patentable subject matter then the method claims that have been withdrawn may be rejoined and examined in this one application provided the method of use recite limitations corresponding to those found to be patentable during examination of the elected invention. As such, when the product claims are found to recite patentable subject matter, non-elected method claims 11, 12, 15-18, 23, 25, 27, 30, 33, 35, and 37-47 should be taken up for examination.

Fees Payable

No fee is due for entry of this response, however, if a fee is found due, the Commissioner is authorized to charge such fee to Deposit Account No. 13-4365 of Moore & Van Allen.

Conclusion

Applicants have satisfied the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §112. It therefore is requested that Examiner Carter reconsider the patentability of the pending claims in light of the distinguishing remarks herein, and withdraw all rejections, thereby placing the application in condition for allowance. If any issues remain outstanding incident to the allowance of the application, Examiner Carter is requested to contact the undersigned attorney at (919) 286-8089.

Respectfully submitted,

Marianne Fuierer

Marianne Fuierer
Reg. No. 39,983

Attorney for Applicants

Moore & Van Allen, PLLC
Telephone: (919) 286-8000
Facsimile: (919) 286-8199